Topic: Automatic Identification of Critical Areas of the Head and Neck for Refined Dose-Toxicity Analysis in Radiotherapy

Goal: Design, implement, and evaluate an algorithm that creates spatially dependent dose features at the inter-organ level to identify specific areas of the head and neck that are more or less critical and sensitive to radiation damage.

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Mentor: Dr. Todd McNutt

Statement of Relevance/Importance:

Radiation therapies are designed to minimize radiation exposure to areas outside the tumor to avoid adverse reactions to radiation therapy, such as swallowing impairment and speech damage. However, not much is known about which anatomical regions most increase or decrease the probability of specific adverse effects when exposed to radiation- there may be areas in the soft tissue that are absolutely critical to avoid. Currently, specific known structures can be avoided by contouring them semi-automatically from CT image data and planning radiation therapies to avoid them. It would take too much time to contour all structures in the complex head and neck anatomy, so we plan to develop an algorithm to define anatomical regions in the head and neck based on proximity to already-contoured structures. This software will be used in combination with machine learning algorithms to determine which of the specific areas in the head and neck are more or less critical and sensitive to radiation damage, to better assist in the planning of radiation therapy to minimize adverse effects.

Technical Summary of Approach:

We plan to use a deformable registration to create an “average patient” from the subset of patient data, where all contoured structures are available. This registration will likely be taken from one of a number of openly available tools. As part of our roadmap objective for March 3rd, we will decide on a suitable registration method, as well as any conversions from the database’s binary mass structures to new data structures that are necessary (such as a surface mesh, etc.).

We will pick a subset of contoured anatomy that exists in the database to use as reference for the creation of an atlas. The structures capable of being outlined by this atlas will be determined by the contoured structures in the database. A coordinate system will be established that uses fixed points within these structures (e.g. via a center of calculated mass algorithm) to establish vectors that can be used to establish axes. From there, the analysis of any particular input CT will work via a transformation of the atlas anatomical coordinate system to match the location of already contoured structures in the patient. We will use a subset of the database to validate this approach by measuring the error (either by the dice coefficient analysis, and/or by an average distance) between the automatically detected contours and a testing set of manually contoured anatomical features.

Finally, we have been given access to code written to evaluate dose-volume histograms from the database and from treatment parameters. If possible, as the max deliverable, we will integrate this dose-volume component into a graphical user interface along with our anatomical atlas segmentation system, in order to present a concise and simple program to a user.

Deliverables:
Min: *Well-documented* API for automatically detecting verified relevant features in contoured anatomy, written in Python / C++.
Expected: Automated script to add new points of fixation and evaluate either improvement or worsening of predictive power of the coordinate system, in addition to minimum deliverable.
Max: GUI to view ROI estimates along with dose volume histogram of carved regions in addition to the expected and minimum deliverables.

Timeline:

Objective	**Dates**	**Proof of Completion**
Begin work on Min Deliverable	2/13 – 3/31	(see below)
Literature search, project presentation/plan complete.	2/13 - 2/21	N/A
Familiarize with existing code base, complete overall roadmap of expected code, including classes, program structure, and expected methods of code validation.	2/21 - 3/3	UML Diagrams for all major programs, including a defined mathematical method for the construction of the reference atlas.
Create program to consolidate known structures from database into a reference atlas, with a base coordinate system defined on contoured structures.	3/3 - 3/31	Files containing a collection of binary masks representing important anatomy, with metadata containing information regarding their relative locations and orientations.
Construction of a program that registers a patient CT and creates a transformation matrix between the anatomical reference coordinate system and the CT coordinate system, allowing the outline of regions of interest.	3/3 - 3/31	Code that on input of a set of binary masks with metadata and a CT creates a series of binary masks representing anatomical regions of interest
Validation method for deliverable 1 that calculates the error between automatic delineation of regions of interest and	3/3 - 3/31	Program that compares binary masks and uses either dice coefficient analysis or average squared distance to provide an error metric for the

physician-outlined regions of interest from the database.		difference between automatically computed anatomical regions, and physician detected regions.
Completion of Min Deliverable	3/31	
Begin Deliverables 2 & 3	4/1 - 5/18	
Create script to allow users to designate new points of reference in the atlas (which would be used to determine coordinate transformations between patient CT and the atlas)	4/1 - 4/14	Script that changes metadata in the anatomical reference files to include new points of reference, and that changes the registration script so that it uses these points of reference.
Add a validation program that takes the atlas with added reference points, computes its performance in the same manner as the validation step for deliverable 1, and removes the reference points if performance decreases.	4/14 - 5/5	A script that provides error comparison between different atlas configurations.
Deliverable 2 Complete	5/5	
Create a GUI that integrates dose-volume histograms with automatically detected regions of interest.	4/14 -5/18	A working GUI that presents dose-volume histograms for specified regions of interest with estimated error metrics.

Dependencies and Plan for Resolving:

- Access to anatomy database and pre-written python code for decompressing and displaying the data. (Complete, 2/19)
- Install CRKit (Computational Radiology Kit, free from Harvard Medical). (Complete, 2/20)
- Find optimal deformable surface registration algorithm. (Discuss with Dr. Taylor, Dr. McNutt, and their students, lit search; plan to complete by 3/3)

Management Plan:

- Weekly meetings with Dr. McNutt
- Julie, Arun will work on atlas development + mapping to patient anatomy
- Chris will work on validation pipeline

Reading List:

Han, X. et al. (2008). Atlas-based auto-segmentation of head and neck CT images. In: Metaxas D., Axel L., Fichtinger G., Székely G. (eds) Medical Image Computing and Computer-Assisted Intervention – MICCAI 2008. MICCAI 2008. Lecture Notes in Computer Science, vol 5242. Springer, Berlin, Heidelberg

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Commowick, O., Grégoire, V., Malandain, G. (2008). Atlas-based delineation of lymph node levels in head and neck computed tomography images. *Radiotherapy and Oncology*, 87(2), 281-89. ISSN 0167-8140, http://dx.doi.org/10.1016/j.radonc.2008.01.018.

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Zhang, T., Chi, Y., Meldolesi, E., Yan, D. (2007). Automatic delineation of on-line head-and-neck computed tomography images: Toward on-Line adaptive radiotherapy. *International Journal of Radiation Oncology*Biology*Physics*, 68(2), 522-30. ISSN 0360-3016, http://dx.doi.org/10.1016/j.ijrobp.2007.01.038.

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Han, X., Hibbard, L.S., O'Connell, N., and Willcut, V. (2009). Automatic Segmentation of Head and Neck CT Images by GPU-Accelerated Multi-atlas Fusion, *MIDAS Journal*. http://www.insight-journal.org/browse/publication/685.

- https://www.researchgate.net/profile/Lyndon_Hibbard/publication/228519091_Automatic_Segmentation_of_Parotids_in_Head_and_Neck_CT_Images_using_Multi-atlas_Fusion/links/0deec516d54dfccb97000000.pdf

Warfield, S., Zou, K., Wells, W. (2004). Simultaneous truth and performance level estimation (STAPLE): An algorithm for the validation of image segmentation. *IEEE Trans. Med. Imag.* 23(7) 903–921

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Teng, C., Shapiro, L. G., Kalet, I. (2006). Automatic segmentation of neck CT images. Proc. 19th IEEE International Symp. on Computer-Based Medical Systems (CBMS).

- http://grail.cs.washington.edu/wp-content/uploads/2015/08/teng-2006-aso.pdf